

**HL7 SPL Working Group Process Communication Forum Telecon
Wednesday, June 4, 2011**

Check out the SPL Working Group WIKI @:
<http://spl-work-group.wikispaces.com>

Questions on SPL:

ER/DL regulatory questions? Send to edrls@fda.hhs.gov

SPL technical questions? Send to spl@fda.hhs.gov

UNII or SRS questions? Send to fda-srs@fda.hhs.gov

As of June 1, 2011: DailyMed has over 24,300 SPL loaded.

Minutes:

Q&A with PILLBOX Project Manager David Hale

Federal Register notice: <http://www.gpo.gov/fdsys/pkg/FR-2011-05-23/pdf/2011-12629.pdf>

Link to WIKI PILLBOX FAQ page: <http://spl-work-group.wikispaces.com/PILLBOX+FAQ>

Mailbox: The address for PILLBOX@mail.nih.gov

David Hale monitors this mailbox. So if you want more background, or want to discuss the project further, send an e-mail to that mailbox. Alternatively, you can contact him at (301)-496-3042

From the Federal Register Notice: NLM has established Pillbox, an initiative to enhance patient safety, by making available via a publicly accessible resource (<http://pillbox.nlm.nih.gov>) digital images and descriptive data of solid oral dosage form medications (e.g., capsules and tablets, also referred to as "pills"). NLM intends to create a search system allowing patients, healthcare providers, and the public to identify and reference medications using the submitted images and related descriptive information. Such a resource is intended to have application in poison control, emergency response, disaster response, anti-counterfeiting, manufacturer compliance with Federal regulations, improved prescription filling accuracy, and reduction of medication errors and adverse drug events.

The NLM wants to make this information more accessible to everyone as part of the OpenSource initiative. Both FDA & NLM are very excited about the outcome of this project – that standardized product images coming from the firms will be available in the SPL for viewing by users. Images are used in all pharmacy aspects. They have become integral to the practice of pharmacy

An analysis of current SPL data indicated that 14,763 solid dose form product presentations are possibly in scope. PILLBOX data will be pulled from DailyMed, so we're working to create and maintain the flow of images. We will reflect current information. As part of this push towards implementation, the current beta site of PILLBOX will be shut down as soon as we begin receiving images from DailyMed.

Questions and Answers:

Q1: When will the IG be updated to provide instructions on how to include these files?

A: Already available in the current Implementation Guide (SPL Implementation Guide for FDA Drug Establishment Registration and Drug Listing v2.0) in section 3.1.11. *Product characteristics (pg 15)*

<http://www.fda.gov/downloads/ForIndustry/DataStandards/StructuredProductLabeling/UCM162024.pdf>

Q2: Will the FDA eventually require these image files to be included in SPL?

A: This is a question for the FDA. Currently, inclusion of these image files is voluntary.

From the Federal Register Notice: *Participating organizations will be invited to submit samples of their solid oral dosage form medications to NLM for imaging. Resulting image files will be provided to participants, who may choose to voluntarily include them in their subsequent SPL submissions to FDA. Image files that are voluntarily submitted to FDA as part of an SPL listing submission will be included in the publicly accessible, production version of Pillbox.*

From NLM perspective, they see the value in this and they are very excited about being part of the roll-out. They are trying to prove the usefulness of having this information available.

Q3: Have you gotten any samples yet?

A: Yes.

NLM is currently **working on their policy on how they will let people know of a company's willingness to participate in the imaging project.**

Q4: How many companies have indicated that they are planning to send samples (so far)?

A: Yes – we have heard from 4 firms [as of June 1]

NLM is currently **working on their policy on how they will let people know of a company's willingness to participate in the imaging project.**

Have received samples from 2 firms.

Q5: Posting the names of the companies involved in the process? Are you thinking of including a list of the products provided by each of the companies?

From the Federal Register Notice: *Manufacturers, including repackagers, and private label distributors who participate in this process will be acknowledged on the Pillbox Web site and in other communications about the project.*

NLM is trying to figure out how to do this. Some firms are just hearing about this and it takes time to determine if a firm wants to participate. They are not posting this currently, but will do this soon. They want to make sure that firms have time to respond.

At a very least, they will participate the names of the firms on the Pillbox site and in various communications. They want to be transparent about this.

NLM would like feedback on this.

Q6: Can you accept controlled substance samples?

A: Yes. If you are planning to send controlled substances, contact pillbox@mail.nih.gov to obtain the relevant license information needed for the shipping of these products.

ie DEA number, etc.

They were informed not to include DEA number in the Federal Register Notice.

From the Federal Register Notice: NLM, in collaboration with FDA, has set up a photography laboratory at an FDA facility in Rockville, Maryland for the purpose of generating standardized images of representative solid oral dosage form medications for the duration of this project. This facility is registered with the Drug Enforcement Administration.

Q7: Have you started taking photographs yet?

A: Not yet. As soon as the Federal Register Notice was published, we were able to start the process of reactivating the laboratory and contract. This process is now underway.

Contract said that could not take photos until the Federal Register Notice was released. They now have to set up the process.

Q8: Can I take my own photographs and send them in the SPL file?

A: Currently that is outside the scope of the Federal Register Notice. If this is something that you wish to explore further, you may want to contact the FDA at spl@fda.hhs.gov to discuss further.

Q9: Will your methodology for taking these photos be made public?

A: Yes. The methodology will be made public.

From the Federal Register Notice: To remedy this situation, NLM, working with FDA, has developed a standardized methodology for creating digital images of solid oral dosage form medications

Q10: How long will it take to get images back from NLM?

A: The turnaround time is based on resources. A sustained level of participation from sponsors & the number of available photographers will contribute to reduction of turn-around time.

Depends on the volume of samples that are received. Hope to be able to scale the resources, as needed.

Q11: What will the image look like?

A: Right now, the specification is very simple. The image will be presented on a 18% gray background, with obverse and reverse displays for a tablet, and two rotations that allow the markings on the capsule to be displayed for a capsule. There is still discussion on whether to include a 'fiduciary' (a ruler or measurement presented as part of the image file).

Issue of 'fiduciaries' (rulers or measurements on the image) –

The image is a data element of the product. The ruler on the image has become a topic of discussion – as to whether that is an inclusion of a data element. Main concern is that that data is included in the listing information, and the image is supposed to be free of data elements from the SPL. **Should it be part of the image?** We want the image to be viewed in terms of the SPL. The images are easier to look at without the rulers (nothing gets in the way of the image of the solid oral dosage). Also, when you scale the photo with the ruler present, if you scale up or down, the ruler can be distorted.

Q12: How many files will we get back for each sample?

A: For each sample, ideally we'd like to send two files:

- an uncompressed, color-corrected image of a rather large size (color corrected, more perfect image). This level of quality is key to downstream uses.
- JPG rendition of the master image – it has to be less than 150K size for SPL.

The National Library of Medicine would like firms to validate the master image and then verify that the JPG is an accurate representation of the larger file. The JPG will be attached to the SPL.

From the Federal Register Notice: *In order to test the imaging methodology in an operational setting and to begin developing a production version of Pillbox, NLM is offering, on a time-limited basis, to provide manufacturers, including repackagers, and private label distributors who send product samples to NLM, image files suitable for inclusion with their SPL files that are being submitted to FDA.*

Q13: What is the format of the larger size file?

A: The larger image format will be an uncompressed file of PNG format- portable network graphics -- with color space intact. Data is not compact and it maintains the integrity of the color. New standard for web imaging.

Can never use jpg for print because not necessarily accurate. It just appears to be the right color to humans.

Q14: Why do you need more than 1 of each sample?

A: We want to make sure we get the most aesthetically pleasing example. Some of the “pills” have scratches, blemishes, etc. They sort through all the samples to get the most pristine example.

From the Federal Register Notice: *Select and ship the smallest volume stock package(s) totaling at least 8–10 representative solid oral dosage form medications (e.g., tablets, capsules) of the same drug product. In order to ensure the safety of facility staff and compliance with appropriate federal regulations please include the accompanying prescribing information.*

If there is a logistic or financial burden with providing 8-10, then contact NLM to discuss.

Q15: When will the FDA start accepting these image files?

A: This is a question for the FDA.

The SPL group should contact FDA and publish this response in central place. FDA currently has responded that this would be a rapid uptake, once they start receiving images. NLM is currently not taking photographs and FDA is waiting for images. They will have to compare/match the filename of the image in the SPL --to the filename of the image provided by NLM.

NLM is close to having the filename issue resolved.

Q16: What kind of file format will the FDA be looking for with the SPL_IMAGE?

A: This is a question for the FDA. However, in the current implementation guide, section 3.1.11.

Product characteristics (pg 15)

<http://www.fda.gov/downloads/ForIndustry/DataStandards/StructuredProductLabeling/UCM162024.pdf>

The xml example describing the SPLIMAGE makes reference to a JPG file:

```
<subjectOf>
  <characteristic classCode="OBS">
    <code code="SPLIMAGE" codeSystem="2.16.840.1.113883.1.11.19255"/>
    <value xsi:type="ED" mediaType="image/jpeg">
      <reference value="file name.jpg"/>
    </value>
  </characteristic>
</subjectOf>
```

Q17: How will the file be named?

A: NLM and FDA are finalizing the details of the filenames. Most likely be like a GUID. One possibility is a 128 bit hexadecimal string (otherwise known as a GUID) unique to the image.

Q18: Are you accepting samples of prescription products?

A: Yes, we are accepting prescription product samples.

Q19: Are you accepting samples of over-the-counter products?

A: Yes, we are accepting over-the counter product samples

Q20: Are you accepting samples of homeopathic products?

A: Yes, we are accepting homeopathic product samples

Q21: Are you accepting samples of veterinary products?

A: Yes, we are accepting veterinary samples

From the Federal Register Notice: *Manufacturers, including repackagers, and private label distributors of prescription and over-the-counter solid oral dosage form medications may submit products for imaging.*

Q22: Who would provide the samples?

A: The manufacturer is responsible for providing the samples

From the Federal Register Notice: *Manufacturers, including repackagers, and private label distributors of prescription and over-the-counter solid oral dosage form medications may submit products for imaging.*

Homeopathics are considered OTC.

Notice does not specify human versus veterinary.

Q23: Can I provide unpackaged samples, such as quality lots?

A: National Library of Medicine requests that you send small volume stock packaging and not yet expired.

From the Federal Register Notice:

- *The expiration date on the submitted products' packaging should be the longest available expiration date.*
- ...
- *Select and ship the smallest volume stock package(s) totaling at least 8–10 representative solid oral dosage form medications (e.g., tablets, capsules) of the same drug product. In order to ensure the safety of facility staff and compliance with appropriate federal regulations please include the accompanying prescribing information.*

Don't know. How would they be packaged? Would the USPI accompany the samples?

NLM is sensitive to the fact that they don't want to request information from sponsors multiple times.

And NLM needs insure safety of people

Controlled substance?

Storage information/handling.

This information is already provided on the packaging/USPI. Therefore they don't have to ask sponsors to fill out another form.

Q24: Do we need to resubmit a new photograph every year?

A: This is a question for the FDA. Currently, inclusion of these image files is voluntary.

This is currently a volunteer effort; companies are not required to submit SPLIMAGE files at this time.

Sponsors are encouraged to keep the photographs included in the SPL up-to-date by obtaining new image files when a product is added or its oral dosage form characteristics have changed.

Q25: What about 'drugs for further processing' – would images help for Imports?

A: This is a question for the FDA.

David has not heard any discussion on this. Drugs for further processing don't go to Daily Med. This could be helpful during Import. But this is not in any regulations, guidances.

Q26. Please explain what is going on with fiduciary representation.

A. NLM envisions the image as just another data element, not a full data package that contains its own metadata. This is consistent with the SPL instructions in the IG.

Data can be inferred just by looking at the image – shape, color. However, you can't determine the actual size. So NLM is discussing whether there should be a ruler or some other fiduciary displayed.

Most government size data are specified only down to the whole number of mm.

Currently, there are two choices:

1. No fiduciary. Nothing that will help establish the size of the product. Must depend on the SPL data.

2. True fiduciary. A scale would be displayed that will represent the scale, eg dots that shows a standard distance (eg 0.1 mm). This does not make a measurement. The viewer would have to extrapolate from the dots to determine the actual size.

NLM would like feedback on this.

Q27: Where will this image be displayed in the browser view of the file.

A. Several people have experimented in inserting images into the SPL, following directions in the IG. The file is valid but Pragnatic Validator doesn't like it. The picture is displayed between the DLDE section and the manufacturing information.

To do: Please test out what happens if there are multiple images provided. Do they appear in one clump. How would a viewer know which image pertains to which set of drug product.

Survey questions to Sponsors:

1. What's your level of comfort for a master list to be put on the PILLBOX website?
2. Are you amenable to validating a master file and verifying that the smaller JPG file is a rendition of the master file acceptable for submission in SPL to the FDA?
3. Do you feel it important to include a fiduciary as part of the image, now that you are aware that it was applied during the production process and may not scale if the image is enlarged or shrunk?
4. Downstream users such as FirstDataBank, Walters-Kluwer and others are eager to see a 'single-stream source' for product images. What could they do to encourage manufacturers to provide these images in the SPL files?